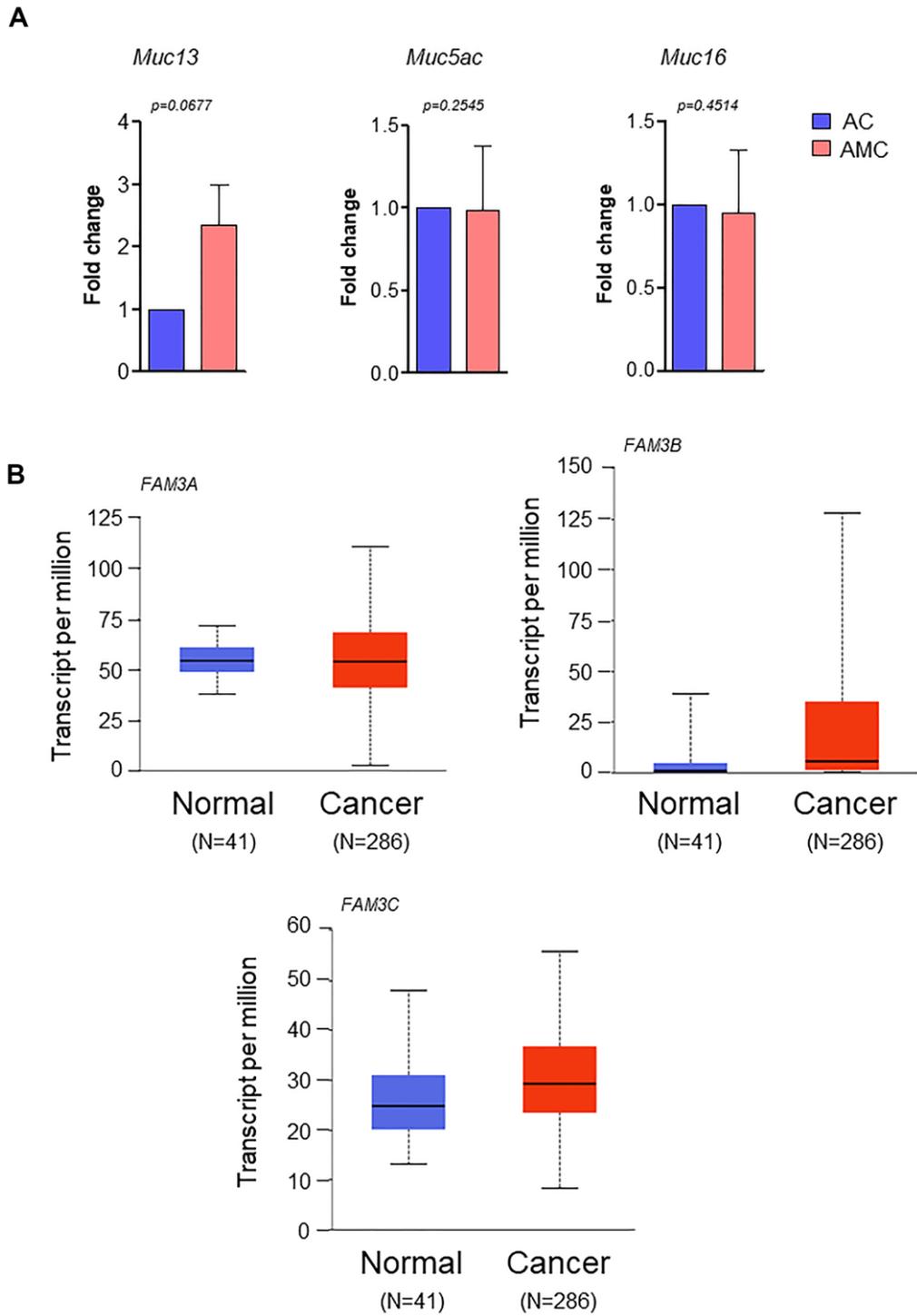
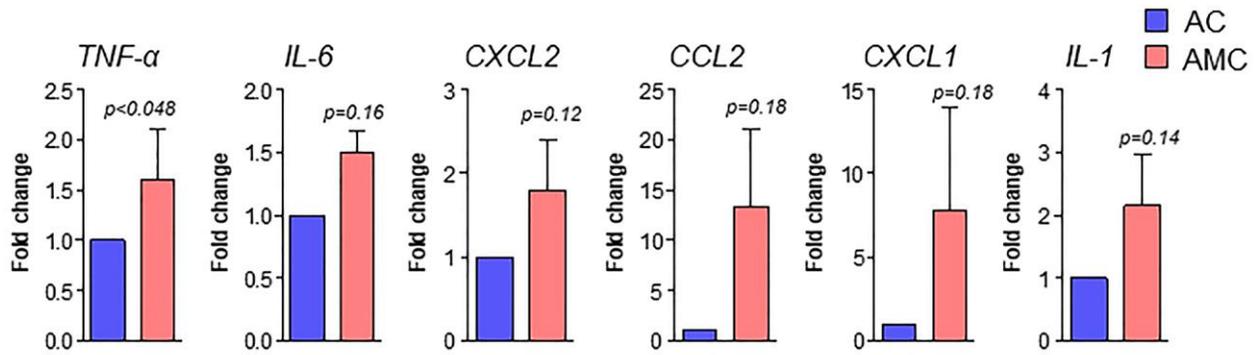
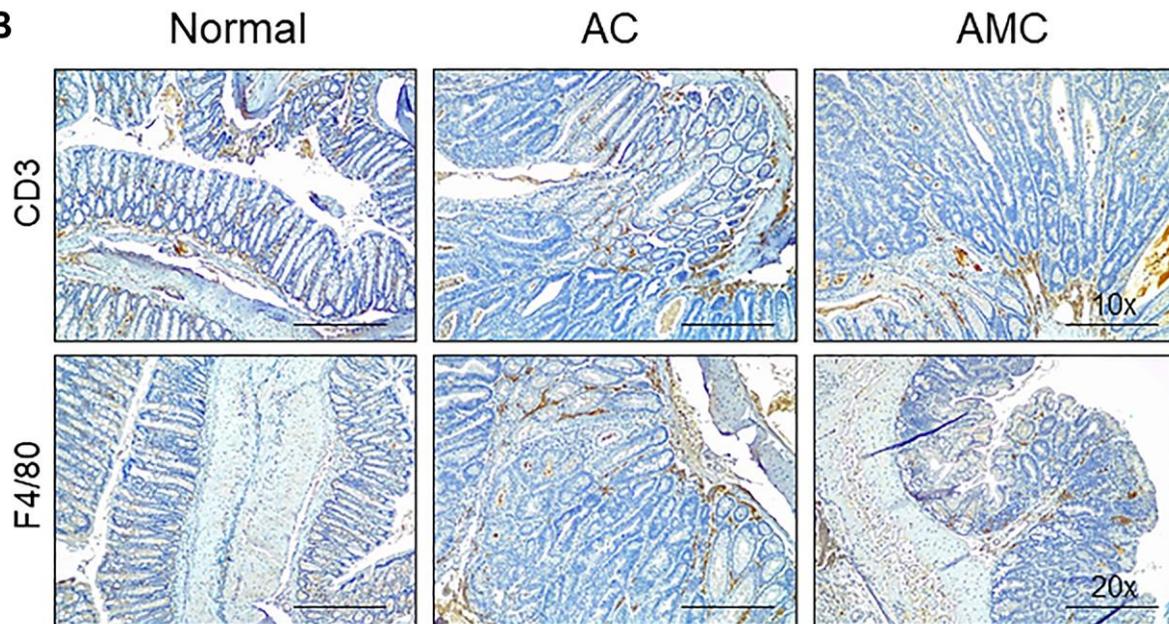


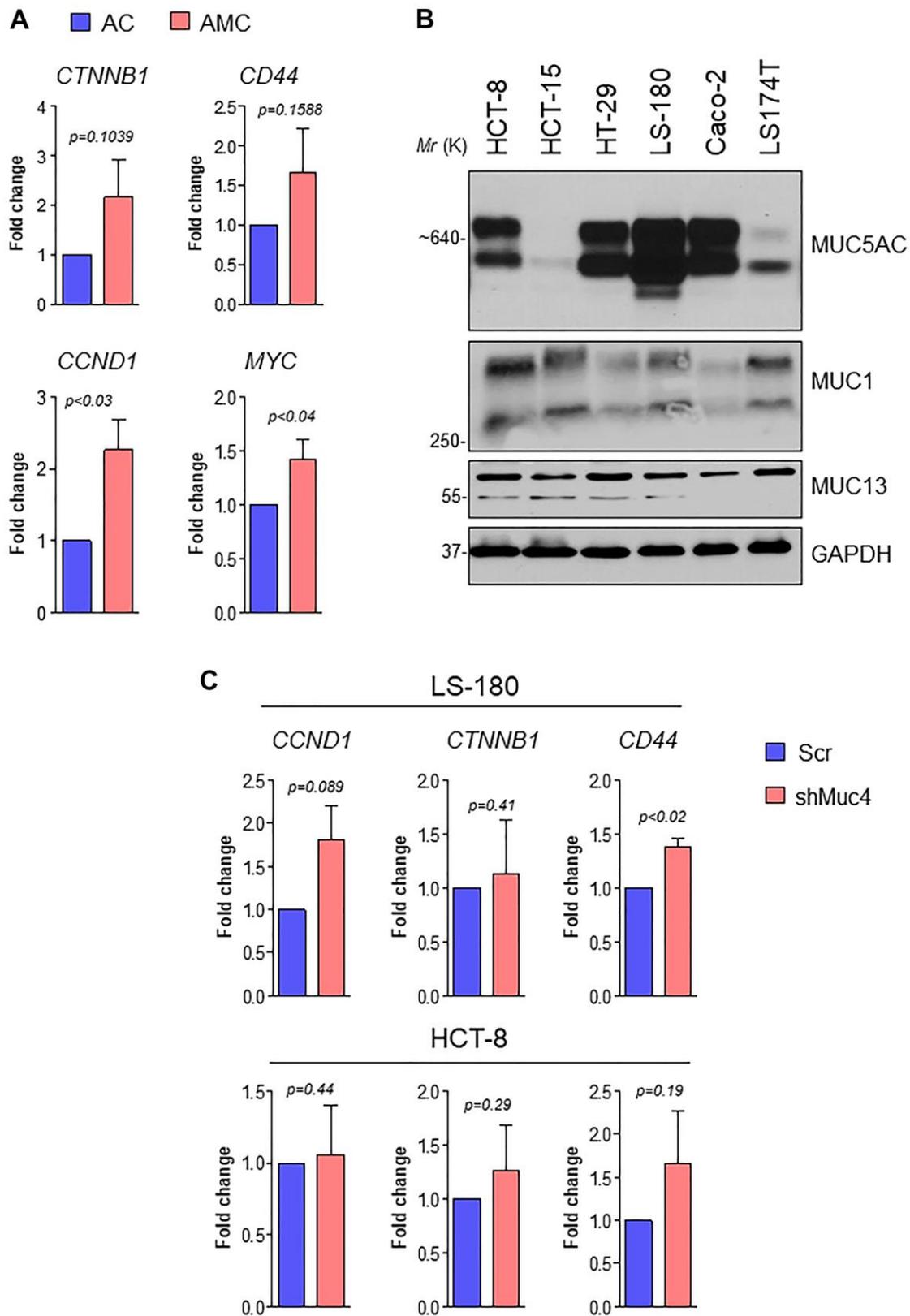
SUPPLEMENTARY FIGURES



**Supplementary Figure 1. The absence of Muc4 alters other mucins and FAM3 expressions.** (A) mRNA expression levels of transmembrane (*Muc13*, *Muc16*) and secreted mucin (*Muc5ac*) in the colons of AC and AMC mice measured by real-time PCR. n = 4 per group. (B) TCGA-COAD expression analysis of FAM family members (*FAM3A*, *FAM3B*, and *FAM3C*).

**A**Pro-inflammatory cytokines**B**

**Supplementary Figure 2. Loss of Muc4 showed changes in the expression of cytokines and inflammatory markers. (A)** mRNA expression levels of proinflammatory cytokines (*Tnfa*, *Il-6*, *Cxcl2*, *Ccl2*, *Cxcl1* and *Il-1*) in the colons of AC and AMC mice measured by real-time PCR.  $n = 3-4$  per group. **(B)** Immunohistochemical staining of immune filtration markers ( $CD3^+$  and  $F4/80$ ) in normal, AC, and AMC mice.  $n = 6$  (AC and AMC) and  $n = 3$  for normal group.



**Supplementary Figure 3.** The absence of Muc4 mediates upregulation of  $\beta$ -catenin and its target genes (A) mRNA expression levels of *Ctnnb1*, *Cd44*, *Ccnd1*, and *Myc* in the colons of AC and AMC mice measured by real-time PCR. n = 4 per group. (B) Screening different types of mucins (MUC5AC, MUC1 and MUC13) in a panel of CRC cell lines by western blot. (C) mRNA expression levels of *CCND1*, *CTNNB1*, and *CD44* in Scr and MUC4-KD CRC cell lines (LS-180 and HCT-8) measured by real-time PCR. n = 3 per group.